CLAIMS

1. Use of an inhibitor of cell development in a controlled manner to maintain the non-differentiated state of stem cells, in particular human stem cells, while allowing their cell division.

2. Use of an inhibitor according to claim 1, in which the stem cells are human cells chosen from the group consisting of embryonic stem cells at the origin of somatic stem cells, and/or the stem cells/somatic progenitors themselves at the origin of blood and/or various solid tissues, such as the skin, the liver, the pancreas, the heart, the kidney, bone or nerve tissue.

sub Q1

3. Use of an inhibitor according to claim 1 or claim 2, in which the inhibitor of cell development is chosen from the group consisting of products of genes which control cell development with respect to cell differentiation and/or cell division, inhibitors of cycline-dependent kinases, factors which control apoptosis or ageing, and cytokines (such as interferons and TGF-β).

4. Use of an inhibitor according to any one of claims 1 to 3, in sequential combination with an anti-inhibitor of cell proliferation, to initiate a number of cell divisions ranging from 1 to about 100, in particular 1 to about 10, and in particular to initiate a single cell division, while maintaining the non-differentiated state of stem cells, in particular human stem cells.

5. Process for the multiplication of stem cells in a culture medium, in particular human stem cells, characterized in that it comprises:

– a stage in which the stem cells, in particular human stem cells, in the resting state are brought out of their resting state by neutralization of the effect of an inhibitor of cell development, and in particular an inhibitor of cell proliferation, produced by the cells and/or present in the culture medium so that there is initiation of a number of cell divisions ranging from 1 to about 100, in particular 1 to about 10, and in particular a single cell division,

– and a stage in which the stem cells, in particular human cells, obtained in the

preceding stage are inhibited in their differentiation with the aid of an inhibitor of cell development.

6. Multiplication process according to claim 5, characterized in that at the end of the multiplication process the stem cells multiplied in this way are maintained in a non-differentiated state.

7. Multiplication process according to claim 5, characterized in that the stem cells are human cells chosen from the group consisting of embryonic stem cells at the origin of somatic stem cells and the somatic cells themselves at the origin of blood and/or various solid tissues, such as the skin, the liver, the pancreas, the heart, the kidney, bone or nerve tissue.

Sub Q2 **8.** Multiplication process according to one of claims 5 to 7, characterized in that the stem cells, in particular human cells, are present in a cell concentration of about 1 to about 10^{10} cells per ml, and in particular in a concentration ranging from about 10^3 to about 10^{10} cells per ml, and more particularly about 10^4 to about 10^9 cells per ml.

9. Multiplication process according to any one of claims 5 to 8, characterized in that the inhibitor of cell development is synthesized by the stem cells, in particular human stem cells, and/or is added to the culture medium containing the stem cells, in particular human stem cells.

10. Multiplication process according to any one of claims 5 to 9, characterized in that the inhibitor of cell development is chosen from the group consisting of products of genes which control cell development with respect to cell differentiation and/or cell division, inhibitors of cycline-dependent kinases, factors which control apoptosis or ageing, and cytokines (such as interferons and TGF-β).

11. Multiplication process according to any one of claims 5 to 10, characterized in that the inhibitor of cell development is present in a low concentration in the culture medium containing the stem cells, and in particular in a concentration ranging from about 10^{-10} mg/ml to 1 mg/ml.

12. Multiplication process according to any one of claims 5 to 11, characterized in that the neutralization of the effect of the inhibitor of cell development, and in particular the inhibitor of cell proliferation, present in the culture medium is effected by

– addition to the culture medium, in a suitable amount, of an anti-inhibitor of cell proliferation, such as an anti-TGF-β, and/or

– withdrawal from the culture medium of the inhibitor of cell development, and in particular the inhibitor of cell proliferation, belonging in particular to the cytokine group.

13. Multiplication process according to any one of claims 5 to 12, characterized in that the anti-inhibitor of cell proliferation is present in a concentration ranging from about 10^{-18} to about 10^{-3} g/ml.

14. Multiplication process according to any one of claims 5 to 8, in which the culture medium contains hematopoietic stem cells and comprises one or more cytokines (added to the culture medium) chosen from the group consisting of interleukins and CSF, the said cytokines being present in a concentration ranging from about 10^{-8} μg/ml to about 1 mg/ml, and in particular about 10^{-5} μg/ml to 0.1 μg/ml.

15. Multiplication process according to any one of claims 5 to 14, characterized in that it comprises the following stages:

a) initiation of a first cycle of division of non-differentiated embryonic or somatic stem cells in a culture medium, and in particular of hematopoietic somatic stem cells, by seeding non-differentiated embryonic or somatic stem cells in the resting state in a high initial cell concentration, in particular in a concentration ranging from 10^3 to 10^{10} cells per ml, in the presence of one or more cytokines, and by neutralization of the effect of the inhibitor of cell development, and in particular the inhibitor of cell proliferation, present in the culture medium so that the above-mentioned cells leave their resting state by the initiation of a first cell division,

b) return to resting of the non-differentiated embryonic or somatic stem cells obtained in the preceding stage with the aid of an inhibitor of cell development, the said inhibitor being synthesized by the said stem cells or being added to the culture medium,

c) if appropriate washing of the non-differentiated embryonic or somatic stem

cells obtained in the preceding stage in order to remove the catabolites and the inhibitor of cell development, and in particular the inhibitor of cell proliferation which may be present in the culture medium,

d) if appropriate dilution of the non-differentiated embryonic or somatic stem cells obtained in the preceding stage in order to maintain an optimum cell concentration ranging from about 100 to 10^{10} cells per ml,

e) successive repetition of the cycles of division and resting described above until the amplification factor of the cells is sufficient to obtain the number of desired stem cells, and in particular 2 times to about 10^{12} times the number of initial non-differentiated embryonic or somatic stem cells, which corresponds to a total duration of the multiplication process of about 1 day to 3 years, and in particular 1 day to 15 days,

f) stopping of the multiplication of non-differentiated embryonic or somatic stem cells to store them, use them or cause them to differentiate *in vitro*.

16. Multiplication process according to any one of claims 5 to 15, characterized in that the duration of a single resting state ranges from about 1 hour to 3 years, and is in particular about 6 hours to 72 hours, and in that the duration of a single division cycle ranges from about 6 hours to 3 years, and is in particular about 6 hours to 24 hours.

17. Use of non-differentiated and amplified human stem cells such as are obtained by the process of any one of claims 5 to 16 to reconstitute human blood and/or human solid tissue or organs.